Ultrasonic-positioned high intensity focused ultrasound
in the ablation of superficial bladder wall in miniswines

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Abstract: In order to simulate the ablation of superficial bladder tumor, the effectiveness of ultrasound-positioned high intensity focused ultrasound (HIFU) on the bladder wall was determined. One part of the bladder wall in 10 miniswines was selected as a damage region using ultrasonic imaging. Then, it was treated with a 1.6MHz extracorporeal spherical-bowl transducer. Animals were killed immediately after treatment and the bladder wall and rectal tissue were examined macroscopically and histologically. As a result, brighter echoic regions at the selective damage of bladder wall were detected by ultrasonic imaging immediately after treatment. These brighter echoes were correspondent to the acute bladder wall damage, which caused obvious necrosis on the superficial bladder wall. Also, histological analysis of the treated areas revealed epithelial denudation, irreversible changes of submucosal and superficial muscular layer. There occurred no macroscopic hematuria and rectal perforation except for one case of small part burn of the rectal wall. It was concluded that as an extracorporeal approach HIFU could be used successfully to sonicate the selective region of the bladder wall in a large animal model.

INTRODUCTION

With the development of imaging techniques, it is currently much safer and more effective to apply HIFU as a minimally invasive surgery in resection of tumors. There have been reports about research using apparatus capable of both ultrasonic imaging and tissue damaging. And such apparatus were used for the study of HIFU applied in destroying large animals' deep-seated organs that are histologically and structurally closet to those of human. In order to simulate the ablation of superficial bladder tumor, miniswines were selected as models in this study to explore the effectiveness and safety of HIFU guided by diagnostic ultrasound in damaging normal bladder wall.

MATERIALS AND METHODS

Animals 10 miniswines were chosen and not given food for 12 hours. Depilation and derosination were performed on the lower abdomen skin following intra-abdominal anesthesia with 3% pentobarbital sodium.

HIFU therapeutic Unit This unit was composed of 5 parts: ultrasound diagnostic and positioning device, combined transducer featuring combination of a diagnostic and a therapy transducer, movement controlling device, and a therapeutic bed attached with a degassed water tank. Computer controlled, the unit is capable of moving in X, Y, Z directions and automatically positioning and treating target tissues. The therapy transducer was developed on the basis of lens focussing theory with focal a volume of 1.1mm×1.1mm×4mm, a frequency u of 1.6MHz, a focal length of 120mm, and an output acoustical power of 5832W/cm².

Ultrasound Sonication The miniswine were lain on the therapeutic bed with its lower abdomen skin in contact with degassed water. Once the bladder became full, using diagnostic scanner, preliminary ultrasonography was performed on all subjects. One part of the bladder wall was selected as a lesion. Then the focal volume of the therapy transducer was shifted to the target area at bladder mucosa. Then a 20-second single pules of HIFU sonication was finished. After the sonication, using diagnostic transducer to detect iconogrpahical changes before and
after HIFU treatment, the area under treatment and the degree of lesion were determined. Following treatment the pig was sacrificed. The bladder was exposed after laparotomy. 10ml urine was drawn and examined. The bladder wall was carefully examined macroscopically and histologically.

RESULTS

Urine examination  no macroscopically hematuria was visible. In two cases out of ten was macroscopically hematuria.

Ultrasound images  Following treatment, the bladder was re-scanned with diagnostic ultrasound to look for lesions. In nearly all the miniswines there was an increased ecogenicity at the surface of target wall. On opening the bladder it was correspondent to the acute bladder wall damage which caused obvious necrosis on the surface of the wall.

Morphological changes in the damaged bladder wall  The lesions had pale centers surrounded by a 2mm ring of superficial hemorrhage. The surrounding bladder musosa was edematous for a further 8mm from the outer edges of the hemorrhage. A clear demarcation was seen between the damaged and the surrounding tissues. Lesions extended to mucosa and the lamina propria, which were in forms of epithelial denudation and scattering residuals of degenerating necrosed basal cells. Hydrops appeared in the lamina propria, which had no clear demarcation with submucosa. There local occurred also hemorrhage and obvious blood extravasation. Lesions were detected with electron microscope in mucosa, submucosa and also superficial muscles. The most conspicuous changes were observed in capillary vessels and veinlets where severe extravasation was seen.

DISCUSSION

The hyperthermia and cavitation effects caused by HIFU are crucial to tissue damage. They could bring lesions, epithelial necrosis and denudation. A clear demarcation of lesions could be seen between the lesion and the surrounding tissues. The lesions only reached superficial muscular layer. It suggested that the use of HIFU in the treatment of bladder cancer is feasible if pre-treatment positioning with diagnostic ultrasound is accurate. The large amount of damage in small vessels and extravasation in lumens detected by electron microscope further suggested that the two effects might cause anemia and necrosis in tumors and strengthen the destructive force of HIFU on tumors.

In order to improve on the safety of HIFU utilization, it is necessary to keep the bladder full before treatment. In this study evident changes in ultrasonic images were detected in the target area pre and post treatment, an increase of echogenicity was shown after treatment. The use of B-mode ultrasound scanning offers an important method for the dynamic monitoring of focused ultrasonic effect.